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L2          22 L1 AND "E COLI"

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L3           0 L2 AND ALLERGEN

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L4           0 L2 AND DEAD

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   4 FILES SEARCHED...
L6          12 L5 AND PD<20000406
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L6 ANSWER 1 OF 12 MEDLINE on STN
95046935. PubMed ID: 7958476. Mucosal vaccines based on the use of cholera toxin B subunit as immunogen and antigen carrier. Lebens M; Holmgren J. (Department of Medical Microbiology and Immunology, University of Goteborg, Sweden.) Developments in biological standardization, (1994) Vol. 82, pp. 215-27. Ref: 39. Journal code: 0427140. ISSN: 0301-5149. Pub. country: Switzerland. Language: English.
AB Stimulation of strong mucosal IgA immune responses as a basis for vaccine-induced protection against various pathogens has proved difficult. Most soluble protein antigens administered either parenterally or oral-mucosally have given disappointing results. A notable exception in this regard are cholera toxin (CT) and, particularly in humans, its non-toxic B subunit pentamer moiety (CTB) both of which stimulate a strong intestinal IgA antibody response and long-lasting immunological memory. Based on this, CTB has become an important component in recently developed oral vaccines against cholera and diarrhea caused by enterotoxigenic E. coli. The strong immunogenicity of CT and CTB can to a large extent be explained by their ability to bind to receptors on the intestinal mucosal surface. This has promoted much recent interest in the use of CTB as an oral delivery carrier for other vaccine-relevant antigens. Oral administration of antigens coupled to CTB either chemically or genetically has in several systems been found to markedly potentiate both intestinal and extra-intestinal IgA immune responses against the CTB-coupled antigens and to elicit substantial circulating antibody responses. In contrast to CTB, CT also has strong adjuvant properties for stimulating mucosal IgA immune responses to unrelated, non-coupled antigens after oral co-immunization. This adjuvant activity appears to be closely linked to the A subunit-catalyzed ADP-ribosylating action of CT leading to enhanced cyclic AMP formation in the affected cells.

L6 ANSWER 2 OF 12 MEDLINE on STN
93254204. PubMed ID: 1302285. Extracellular export of Shiga toxin B-subunit/haemolysin A (C-terminus) fusion protein expressed in Salmonella typhimurium aroA-mutant and stimulation of B-subunit specific antibody responses in mice. Su G F; Brahmbhatt H N; de Lorenzo V; Wehland J; Timmis K N. (Department of Microbiology, GBF-National Research Centre for Biotechnology, Braunschweig, Germany.) Microbial pathogenesis, (1992 Dec) Vol. 13, No. 6, pp. 465-76. Journal code: 8606191. ISSN: 0882-4010. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The Shiga toxin B-subunit has been fused to the 23-kD C-terminus of Escherichia coli haemolysin A (HlyA) and exported from attenuated antigen carrier strain of Salmonella typhimurium aroA (SL3261). The expression of the gene fusion under the control of a synthetic modified beta-lactamase promoter (constitutive expression) and under the iron-regulated aerobactin promoter showed that the fusion protein could be stably expressed and exported out of the bacterial cell in significant amounts so long as high copy number plasmids were not used. Oral and i.p. immunization of mice with the hybrid salmonellae resulted in significant B-subunit specific mucosal and serum antibody responses. A comparative analysis of the location of hybrid proteins in the antigen carrier bacterial cell (i.e. cytoplasmic expression and extracellular export) has shown that both modes of expression result in antigen-specific immune responses. This is the first report demonstrating that foreign polypeptides fused to the 23-kD C-terminus of E. coli haemolysin A can be exported from attenuated Salmonella vaccine strains and that such exported polypeptides can result in antigen-specific immune responses.

L6 ANSWER 3 OF 12 MEDLINE on STN
91100317. PubMed ID: 1987133. Expression of the cloned Escherichia coli O9 rfb gene in various mutant strains of Salmonella typhimurium. Sugiyama T; Kido N; Komatsu T; Ohta M; Kato N. (Department of Bacteriology, Nagoya University School of Medicine, Aichi, Japan.) Journal of bacteriology, (1991 Jan) Vol. 173, No. 1, pp. 55-8. Journal code: 2985120R. ISSN: 0021-9193. Pub. country: United States. Language: English.

AB To investigate the effect of chromosomal mutation on the synthesis of rfe-dependent Escherichia coli O9 lipopolysaccharide (LPS), the cloned E. coli O9 rfb gene was introduced into Salmonella typhimurium strains defective in various genes involved in the synthesis of LPS. When E. coli O9 rfb was introduced into S. typhimurium strains possessing defects in rfb or rfc, they synthesized E. coli O9 LPS on their cell surfaces. The rfe-defective mutant of S. typhimurium synthesized only very small amounts of E. coli O9 LPS after the introduction of E . coli O9 rfb. These results confirmed the widely accepted idea that the biosynthesis of E. coli O9-specific polysaccharide does not require rfc but requires rfe. By using an rfbT mutant of the E. coli O9 rfb gene, the mechanism of transfer of the synthesized E. coli O9-specific polysaccharide from antigen carrier lipid to the R-core of S. typhimurium was investigated. The rfbT mutant of the E. coli O9 rfb gene failed to direct the synthesis of E. coli O9 LPS in the rfc mutant strain of S. typhimurium, in which rfaL and rfbT functions are intact, but directed the synthesis of the precursor. Because the intact E. coli O9 rfb gene directed the synthesis of E. coli O9 LPS in the same strain, it was suggested that the rfaL product of S. typhimurium and rfbT product of E. coli O9 cooperate to synthesize E. coli O9 LPS in S. typhimurium.

L6 ANSWER 4 OF 12 MEDLINE on STN
90198517. PubMed ID: 2576522. Oral vaccination of rats with live avirulent Salmonella derivatives expressing adhesive fimbrial antigens of uropathogenic Escherichia coli. Schmidt G; Hacker J; Wood G; Marre R. (Forschungsinstitut Borstel, F.R.G.) FEMS microbiology immunology, (1989 Mar) Vol. 1, No. 4, pp. 229-35. Journal code: 8901230. ISSN: 0920-8534. Pub. country: Netherlands. Language: English.

AB The avirulent Salmonella typhimurium F885 was transformed with a plasmid carrying the cloned S fimbriae genes of a uropathogenic Escherichia coli. The resulting transformant (F885-1) produced efficiently E. coli S fimbriae and was used for live oral vaccination of rats. For comparison rats were immunized subcutaneously with isolated S fimbriae. Both routes of vaccination resulted in a significant IgG antibody response to S fimbriae. In addition live oral vaccination induced a serum IgA response against S fimbriae. After transurethral infection of rats with a S fimbriae producing E. coli a 10-fold reduction of bacterial counts in the kidney was observed in rats orally vaccinated with F885-1 as compared to unvaccinated controls. This study suggests that the avirulent Salmonella F885 may be used as a fimbrial antigen carrier for oral vaccination against renal infections.

L6 ANSWER 5 OF 12 MEDLINE on STN
76033569. PubMed ID: 1101370. Antibody production by human colostral cells. I. Immunoglobulin class, specificity, and quantity. Ahlstedt S; Carlsson B; Hanson L A; Goldblum R M. Scandinavian journal of immunology, (1975 Sep) Vol. 4, No. 5-6, pp. 535-9. Journal code: 0323767. ISSN: 0300-9475. Pub. country: Norway. Language: English.

AB The production of antibody by human colostral cells was assayed by the hemolysis in-gel technique. When sheep erythrocytes coated with O antigens from frequently encountered Escherichia coli bacteria were used as detector cells and anti-IgA serum was added for development, numerous plaque-forming cells (PFC) were demonstrated in all samples tested. In contrast, plaques were rarely seen in the presence of anti-IgG developing serum. The direct (IgM) plaques occasionally noted with both antigen-coated and uncoated sheep erythrocytes were mainly due to the production of heterophil antibodies, since they were not formed when human erythrocytes were used as O-antigen carriers. A strikingly high number of the colostral lymphocytes formed antibodies to the E. coli antigens, up to 8%. This suggests that these cells represent a rather selective population--possibly cells from the gastrointestinal tract exposed to enteric bacteria. The large number of plaques observed, the predominance of the cells forming IgA antibodies, and the marked changes in PFC number in relationship to parturition pose a number of questions relevant to the antibody-producing colostrum cells and their relationship to the secretory immune system.

L6 ANSWER 6 OF 12 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
1989062675 EMBASE Oral vaccination of rats with live avirulent Salmonella derivatives expressing adhesive fimbrial antigens of uropathogenic Escherichia coli.
Schmidt, G.; Hacker, J.; Wood, G.; Marre, R.. Forschungsinstitut Borstel, 2061 Borstel, Germany.
FEMS Microbiology Immunology Vol. 47, No. 4, pp. 229-235 1989.
ISSN: 0920-8534. CODEN: FMIMEH
Pub. Country: Netherlands. Language: English. Summary Language: English.
Entered STN: 911212. Last Updated on STN: 911212
AB The avirulent Salmonella typhimurium F885 was transformed with a plasmid carrying the cloned S fimbriae genes of a uropathogenic Escherichia coli. The resulting transformant (F885-1) produced efficiently E. coli S fimbriae and was used for live oral vaccination of rats. For comparison rats were immunized subcutaneously with isolated S fimbriae. Both routes of vaccination resulted in a significant IgG antibody response to S fimbriae. In addition live oral vaccination induced a serum IgA response against S fimbriae. After transurethral infection of rats with a S fimbriae producing E. coli a 10-fold reduction of bacterial counts in the kidney was observed in rats orally vaccinated with F885-1 as compared to unvaccinated controls. This study suggests that the avirulent Salmonella F885 may be used as a fimbrial antigen carrier for oral vaccination against renal infections.

L6 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
1999:761959 Document No. 132:45567 Expression of CS3 from enterotoxigenic Escherichia coli in Shigella flexneri 2a and immunogenicity of the recombinant strain. Han, Zhaozhong; Ying, Tianyi; Cao, Yong; Rui, Xianliang; Zhang, Zhaoshan; Su, Guofu; Huang, Cuifen (Beijing Institute of Biotechnology, Beijing, 100071, Peop. Rep. China). Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao, 15(5), 719-723 (Chinese) 1999.
CODEN: ZSHXF2. ISSN: 1007-7626. Publisher: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuebao Bianweihui.
AB A host-plasmid balancing system was established based on asd gene in a candidate vaccine strain(T32) of Shigella flexneri 2a. Asd gene of T32 was amplified by polymerase chain reaction(PCR), and its structural gene fragment was replaced by human interleukin 2 gene. The mutated asd gene was introduced to T32 genome by homol. recombination. The resulted bacteria strain (FaD) was used as antigen carrier to express Escherichia coli surface antigen CS3 of enterotoxigenic E

. coli, which was expressed on a complementary plasmid carrying asd gene from Streptococcus mutans. The plasmid could stably be maintained and expressed CS3 in the host cell without any antibiotic selection. Antibodies against CS3 could be detected in sera of mice immunized with recombinant bacteria either orally or s.c., and mice immunized by either route could be protected from challenging with virulent strain of the same serotype. All results indicate that the recombinant constructed can be used as bi-valent vaccine candidate for prevention of bacterial diarrhea.

L6 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
1997:719672 Document No. 128:21852 Immunogenic carrier system against gonadotropin releasing hormone (GnRH). Van Der Zee, Anna; Van Die, Irma Marianne; Hoekstra, Willem Pieter Martin; Gielen, Josephus Theodorus (Akzo Nobel N.V., Neth.). U.S. US 5684145 A 19971104, 28 pp., Division of U.S. Ser. No. 78,661, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-453588 19950530. PRIORITY: NL 1992-1775 19920618; US 1993-78661 19930616.
AB The present invention is concerned with vaccination of mammals against GnRH. The vaccine comprises a GnRH peptide conjugate to E. coli fimbrial-filaments and elicits an immune response against GnRH.

L6 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
1996:123718 Document No. 124:173426 Peptides used as carriers in immunogenic constructs suitable for development of synthetic vaccines. Cohen, Irun R.; Fridkin, Matityahu; Konen-Waisman, Stephanie (Yeda Research and Development Co., Ltd., Israel). PCT Int. Appl. WO 9531994 A1 19951130, 32 pp. DESIGNATED STATES: W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US6575 19950524. PRIORITY: IL 1994-109790 19940525.
AB The invention relates to conjugates of poorly immunogenic antigens, e.g., peptides, proteins and polysaccharides, with a synthetic peptide carrier constituting a T cell epitope derived from the sequence of E. coli hsp65 (GroEL), or an analog thereof, said peptide or analog being capable of increasing substantially the immunogenicity of the poorly immunogenic antigen. A suitable peptide according to the invention is Pep287e, which corresponds to positions 437-453 of the E. coli hsp65 mol. In example, Pep287e was synthesized and conjugated with Citrobacter freundii-derived/protein and nucleic acid and polysaccharide-containing Vi fragment for use as immunogen to stimulate lymph node proliferation.

L6 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN
1992:468120 Document No. 117:68120 Safety, immunogenicity, and efficacy in monkeys and humans of invasive Escherichia coli K-12 hybrid vaccine candidates expressing Shigella flexneri 2a somatic antigen. Kotloff, Karen L.; Herrington, Deirdre A.; Hale, Thomas L.; Newland, John W.; Van de Verg, Lillian; Cogan, John P.; Snoy, Phillip J.; Sadoff, Jerald C.; Formal, Samuel B.; Levine, Myron M. (Sch. Med., Univ. Maryland, Baltimore, MD, 21201, USA). Infection and Immunity, 60(6), 2218-24 (English) 1992. CODEN: INFIBR. ISSN: 0019-9567.
AB A live, oral Shigella vaccine, constructed by transfer of the 140-MDa invasiveness plasmid from S. flexneri 5 and the chromosomal genes encoding the group- and type-specific O antigen of S. flexneri 2a to E. coli K-12, was tested in humans. Designated Ec5f2a-1, this vaccine produced adverse reactions (fever, diarrhea, or dysentery) in 4

(31%) of 13 subjects who ingested a single dose of 1.0 + 109 CFU, while at better-tolerated doses (5.0 + 106 to 5.0 + 107 CFU), it provided no protection against challenge with S. flexneri 2a. A further-attenuated aroD mutant derivative, EcSf2a-2, was then tested. Rhesus monkeys that received EcSf2a-2 in 3 oral doses of 1.5 + 1011 CFU experienced no increase in gastrointestinal symptoms compared with a control group that received an E. coli K-12 placebo. Compared with controls, the vaccinated monkeys were protected against shigellosis after challenge with S. flexneri 2a (60% efficacy). In humans, EcSf2a-2 was well tolerated at inocula ranging from 5.0 + 106 to 2.1 + 109 CFU. However, after a single dose of 2.5 + 109 CFU, 4 (17%) of 23 subjects experienced adverse reactions, including fever (3 subjects) and diarrhea (1 subject), and after a single dose of 1.8 + 1010 CFU, 2 of 4 subjects developed dysentery. Recipients of 3 doses of 1.2-2.5 + 109 CFU had significant rises in serum antibody to lipopolysaccharide (61%) and invasiveness plasmid antigens (44%) and in gut-derived IgA antibody-secreting cells specific for lipopolysaccharide (100%) and invasiveness plasmid antigens (60%). Despite its immunogenicity, the vaccine conferred only 36% protection against illness (fever, diarrhea, or dysentery) induced by exptl. challenge. These findings illustrate the use of an epithelial cell-invasive E. coli strain as a carrier for Shigella antigens.

L6 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

1992:405863 Document No. 117:5863 Regulation of the immune response to hepatitis B virus and human serum albumin. III. Induction of anti-albumin antibody secretion in vitro by C-gene-derived proteins in peripheral B cells from chronic carriers of HBsAg. Hellstroem, U. B.; Sylvan, S. P. E. (Dep. Infect. Dis., Karolinska Inst., Stockholm, S-11489, Swed.). Scandinavian Journal of Immunology, 35(1), 53-62 (English) 1992. CODEN: SJIMAX. ISSN: 0300-9475.

AB The circulatory pool of B cells from the majority (11/13) of chronic hepatitis B surface antigen (HBsAg) carriers contained sensitized B cells with the capacity to secrete IgG antibodies with specificity for human serum albumin (HSA), when stimulated with E. coli -derived core protein at low concns. in vitro. The IgG anti-HSA secretion was dependent upon and regulated by T cells, and optimal secretion was obtained at T/B-cell ratios of 1.0-4.0, varying for different individuals. The level of anti-HSB secretion was higher for patients with on-going viral replication as assessed by hepatitis B virus (HBV)-DNA in serum. Culture supernatants containing anti-HSA antibodies also contained anti-HBc antibodies, as detected by ELISA where the solid phase was charged with E. coli-derived core protein, or the synthetic peptides corresponding to the 75-84 and 132-147 sequences in the C region of HBV. In contrast, IgG anti-HBc (E. coli-derived), but not anti-HSA or anti-HBc 75-84,132 147 antibodies, were detected at similar T/B-cell ratios in cell cultures from 5/6 individuals with naturally acquired immunity to hepatitis B. Thus, peripheral B cells from the majority of HB-immune donors are sensitized to unique (e.g. non-albumin associated) structures in the nucleocapsid of HBV, while B cells in the majority of chronic HBsAg carriers are sensitized to linear C-gene-derived structures in association with the host self-component HSA.

L6 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2008 ACS on STN

1990:476015 Document No. 113:76015 Outer membrane PhoE protein of Escherichia coli as a carrier for foreign antigenic determinants: immunogenicity of epitopes of foot-and-mouth disease virus. Agterberg, Marja; Adriaanse, Henriette; Lankhof, Hanneke; Meloen, Rob; Tommassen, Jan (Inst. Mol. Biol. Med. Biotechnol., Univ. Utrecht, Utrecht, 3584-CH, Neth.). Vaccine, 8(1), 85-91 (English) 1990. CODEN: VACCDE. ISSN: 0264-410X.

AB Outer membrane protein PhoE of E. coli was used for the expression of antigenic determinants of foot-and-mouth disease virus. Five hybrid PhoE proteins were constructed containing different combinations of 2 antigenic determinants of VP1 protein of the virus. The hybrid proteins were expressed in 2 E. coli strains and the proteins were correctly assembled into the outer membrane. The inserted epitopes were exposed at the surface of the cell and were antigenic in this PhoE-associated conformation. Immunization expts., performed with partially purified protein, resulted in all cases in a significant anti-peptide antibody titer. In one case in which the hybrid protein with the largest insert was used, a neutralizing antibody response was detected.

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L7 16 L1 AND ALLERGEN

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L8 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
2007:576104 Document No.: PREV200700573458. Novel recombinant interleukin-13 peptide-based vaccine reduces airway allergic inflammatory responses in mice. Ma, Yanbing; HayGlass, Kent T.; Becker, Allan B.; Fan, Yijun; Yang, Xi; Basu, Sujata; Srinivasan, Ganesh; Estelle, F.; Simons, R.; Halayko, Andrew J.; Peng, Zhikang [Reprint Author]. Univ Manitoba, Dept Pediat and Child Hlth, 715 McDermot Ave, Winnipeg, MB R3E 3P4, Canada. zpeng@ms.umanitoba.ca. American Journal of Respiratory and Critical Care Medicine, (SEP 1 2007) Vol. 176, No. 5, pp. 439-445. ISSN: 1073-449X. Language: English.

AB Rationale: Interleukin (IL)-13 plays a pivotal role in the pathogenesis of allergic asthma. Passive administration of its monoclonal antibody or soluble receptor to block overproduced IL-13 has been proven to be effective in controlling airway allergic responses in animal models, but these approaches have disadvantages of short half-lives, high costs, and possible adverse effects.Objectives: We sought to develop a novel therapeutic strategy through constructing an IL-13 peptide-based vaccine for blocking IL-13 on a persistent effect basis and to evaluate its in vivo effects using a murine model.Methods: To break self-tolerance, truncated hepatitis B core antigen was used as a carrier. Vaccine was prepared by inserting a peptide derived from the receptor binding site of mouse IL-13 into the immunodominant epitope region of the carrier using gene recombination methods. Mice received vaccine subcutaneously three times, and then subjected to intraperitoneal sensitization and intranasal challenge with ovalbumin. Control animals received carrier or saline in place of vaccine.Measurements and Main Results: The vaccine presented as virus-like particles and induced sustained and high titered IL-13-specific IgG without the use of conventional adjuvant. Vaccination significantly suppressed ovalbumin-incluced inflammatory cell number, and IL-13 and IL-5 levels in bronchoalveolar lavage fluids. Serum total and ovalbumin-specific IgE were also significantly inhibited. Moreover, allergen-induced goblet cell hyperplasia, lung tissue inflammatory cell infiltration, and pulmonary hyperresponsiveness to inhaled methacholine were significantly suppressed in vaccinated mice.Conclusions: Our data indicate that IL-13 peptide-based vaccines could be an effective therapeutic approach in the treatment of asthma.

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN

2006:169866 Document No. 144:187529 Carrier for carrying out functional tests on biological cells and method for coating said carrier. Steuer, Heiko; Templin, Markus; Kanzok, Britta; Kuschel, Cornelia; Angres, Brigitte (NMI Naturwissenschaftliches und Medizinisches Institut An der Universitaet Tuebingen, Germany). PCT Int. Appl. WO 2006018072 A1 20060223, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2005-EP7334 20050707. PRIORITY: DE 2004-102004039628 20040810.

AB The invention relates to a method for coating a carrier for carrying out functional tests on biol. cells, to a carrier for carrying out functional tests on biol. cells and to the use of corresponding carriers for carrying out said tests. The process involves (a) the coating of a carrier plate with a hydrogen-bridge donor and/or at least a polycationic substance; (b) applying onto the first layer a hydrogen-bridge acceptor and/or at least a polyanion; (c) immobilizing biomols. and test substances onto the coated layer; (d) incubation with a protein solution; (e) immobilization of cells onto the pretreated carrier. The carrier is glass, plastics, especially polystyrene and/or silicone. Layer (a) is selected from the group of poly-L-lysine, poly-D-lysine, polyamide, aminosilane or their derivs. Layer (b) is nitrocellulose that is applied from a methanolic solution by dipping or spraying. Proteins, especially extracellular matrix proteins, carbohydrates, glycoseaminoglycans, proteoglycans, and lipids are the immobilized biomols. Test substances are antibodies, drugs, messenger mols., growth factors, antigens, and allergens. Test substances are applied by impact or nonimpact printing using a printing buffer with trehalose.

L8 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 1

2005156208. PubMed ID: 15787872. Why Chlamydia pneumoniae is associated with asthma and other chronic conditions? Suggestions from a survey in unselected 9 yr old schoolchildren. Ronchetti Roberto; Biscione Gian Luca; Ronchetti Francesco; Ronchetti Maria Paola; Martella Susy; Falasca Carlo; Casini Carolina; Barreto Mario; Villa Maria Pia. (Pediatric Clinic, Second School of Medicine, Sant'Andrea Hospital, University La Sapienza, Rome, Italy.. ronchetti@uniroma1.it) . Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology, (2005 Mar) Vol. 16, No. 2, pp. 145-50. Journal code: 9106718. ISSN: 0905-6157. Pub. country: England: United Kingdom. Language: English.

AB Despite numerous studies demonstrating an association between asthma and many other chronic conditions and signs of Chlamydia pneumoniae (Cp) infection, the role of Cp in the pathogenesis of these illness remain still unclear. We investigated the prevalence of Cp antigen in the upper airways and the prevalence of detectable Cp serum antibodies in an unselected population of 207 9-yr-old schoolchildren. We also sought the presence of asthma, chronic or recurrent respiratory symptoms by means of questionnaire completed by the parents. Nasal aspirate, blood sampling and allergen skin prick tests were also performed. None of the children had obvious signs of acute infection at physical examination. Cp DNA was detected in nasal aspirates from 20 of the 207 children tested and serum IgG antibodies for Cp in 68 children. No association was found between atopy or history of atopic illness and the presence of Cp DNA or antibody production. This finding is explained by the fact that our study was conducted in an unselected childhood population, inherently including few children with asthma. A strong association between the status of

antigen carrier and the presence of detectable Cp serum immunoglobulin (Ig)G or IgM suggests that subjects with detectable Cp antibodies have an impaired ability to eliminate this pathogen when infected. Because Cp eradication requires a strong Th1 lymphocyte response, the previously proven association between Cp and asthma, might reflect the known association of asthma with Th2-oriented lymphocytic activity.

L8 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
1992:632030 Document No. 117:232030 Suppression of immune responses with oligomeric forms of antigen of controlled chemistry. Dintzis, Howard M.; Dintzis, Renee Z.; Blodgett, James K.; Cheronis, John C.; Kirschenheuter, Gary (Johns Hopkins University, USA). PCT Int. Appl. WO 9211029 A1 19920709, 230 pp. DESIGNATED STATES: W: AU, CA, JP, KR; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US9176 19911217. PRIORITY: US 1990-628858 19901217.
AB A method is provided of specifically suppressing an undesired immune response in a mammal suffering from such a response. The method comprises (1) preparing a construct comprising ≥1 discrete antigenically recognizable moiety (corresponding to a determinant of an antigen causing the undesired immune response) bound to a pharmacol. acceptable carrier, wherein the number of moieties bound to the carrier and the spacing of the moieties on the carrier are such that the construct does not elicit an immune response to the moieties but does directly compete with the antigen for receptors on an immunocompetent cell that recognizes the determinant, the construct thereby specifically suppressing the undesired immune response; and (2) administration of the construct to the mammal in an effective amount Also disclosed are methods for preparing the constructs (scaffold synthesis, conjugate preparation, etc.). A conjugate of dextran with a peptide derivative of a histone H2B amino-terminal fragment was prepared Anti-histone antibody titers in mice that received the suppressive conjugate were suppressed to background levels, while animals receiving control conjugates showed no significant changes (or, in many cases, actual increases) in their anti-histone antibody levels. Animals treated with immunosuppressive conjugate had no detectable cells actively secreting anti-histone antibodies, while control animals had a population of anti-histone antibody-secreting cells too numerous to quantitate. Immunogenicity of a variety of other constructs (e.g. fluoresceinated polymers, benzoylpenicillin conjugate with albumin or with ovalbumin) was examined

L8 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 2
90187904. PubMed ID: 2138201. A method to generate antigen-specific suppressor T cells in vitro from peripheral blood T cells of honey bee venom-sensitive, allergic patients. Carini C; Iwata M; Warner J; Ishizaka K. (Department of Medicine, Johns Hopkins University School of Medicine, Good Samaritan Hospital, Baltimore, MD 21239.) Journal of immunological methods, (1990 Mar 9) Vol. 127, No. 2, pp. 221-33. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.
AB Peripheral blood mononuclear cells of patients allergic to honey bee venom were stimulated with denatured bee venom phospholipase A2, and the antigen-activated T cells were propagated for 4 days by human IL-2 in the presence or absence of recombinant human lipocortin I. Upon antigenic stimulation with the denatured phospholipase A2 and autologous monocytes or by cross-linking of CD3 by anti-CD3 antibody, the activated T cells, which had propagated by IL-2 alone, formed N-glycosylated IgE-binding factors and glycosylation enhancing factor (GEF), while those propagated in the presence of lipocortin formed unglycosylated IgE-binding factors and glycosylation inhibiting factor (GIF). The GEF and GIF formed by the antigen- or anti-CD3-stimulated T cells had affinity for bee venom

phospholipase A2 and could be purified by using anti-lipomodulin Sepharose. In the mouse lymphocyte system, the major cell source of GIF is antigen-specific suppressor T cells, and the antigen-binding GIF from the cells suppressed the in vivo antibody response in an antigen (carrier)-specific manner. In view of the findings in the mouse system, the present results may provide an immunological maneuver to generate allergen-specific suppressor T cells, and to obtain allergen-specific suppressor factor from T cell populations in the peripheral blood of allergic patients.

L8 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
1987:38519 Document No. 106:38519 Original Reference No. 106:6356h,6357a Preparation for the specific modification of the humoral or cellular immune reaction. Theurer, Karl (Fed. Rep. Ger.). Ger. Offen. DE 3513572 A1 19861016, 17 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1985-3513572 19850416.
AB Title prepns. used as carriers to the immune cells, natural soluble antigens, haptenes and allergens, or biomimetically-active antiidiotypic antibodies (European Patent 85102586.6) or sep. or conjugate antideterminant fragments thereof. The carriers can be used for immunosuppression or generation of immuno-tolerance by selective binding of cytotoxic, antimetabolic or alkylating agents, folic acid antagonists, dimeric alkaloids, radionuclides, antihistaminics, etc. The carriers can also be used for specific stimulation of the immune system by selective binding of juvenile lymph node, thymus, bone marrow or spleen exts., informative RNAs of DNAs for antibody formation, etc. Prepns. obtained with this carrier can be used for treatment of multiple sclerosis, myasthenia gravis, post-transplant tissue rejection, etc. Thus, a preparation for the specific immunosuppression of humoral or cellular autosensitization in multiple sclerosis uses as a carrier encephalogenic protein (Kibler, R. F. and Shapira, R., 1968) and myelin from the peripheral nervous system. Protein synthesis-inhibiting agents (erythromycin, chloramphenicol) are adsorbed or bound to the above carrier.

L8 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
1985:339407 Document No.: PREV198580009399; BA80:9399. ENZYME IMMUNOASSAY USING POLYSTYRENE BEADS IN THE DIAGNOSIS OF JAPANESE CEDAR POLLINOSIS. MATSUI S [Reprint author]; NAKAZAWA T; INAZAWA M; UMEGAE Y; KOBAYASHI S; KOCHIBE N; SATO K. FIRST DEP OF INTERNAL MEDICINE, SCHOOL OF MEDICINE, GUNMA UNIVERSITY. Japanese Journal of Allergology, (1985) Vol. 34, No. 1, pp. 6-14.
CODEN: ARERAM. ISSN: 0021-4884. Language: JAPANESE.
AB An enzyme immunoassay (EIA) using polystyrene beads as an antigen carrier and β-D-galactosidase as the enzyme marker was developed for measuring specific IgE antibodies semiquantitatively in Japanese cedar pollinosis. Polystyrene beads can be well coated with the allergen extract from Japanese cedar pollen; ≥ 50 μg protein/ml of allergen is needed for the coating. Reproducibility of this method is acceptable because there was little difference in the results from each bead. Specific IgE antibody levels measured by this method correlated well with those by the radioallergosorbent test (RAST) using paper discs. Inhibition tests using antigen-coated beads and absorbed sera with various kinds of antigens showed that this method is also useful in the detection of activities of fractionated antigens. These results suggest that EIA using polystyrene beads is of value, in place of RAST, in isolation studies of allergen as well as in the diagnosis of Japanese cedar pollinosis.

L8 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 3
83292513. PubMed ID: 6604105. A nylon ball solid-phase radioimmunoassay

for specific antibodies in human sera. Application to measurement of IgG antibodies to pollen allergens. Djurup R; Sondergaard I; Minuva U; Weeke B. Journal of immunological methods, (1983 Sep 16) Vol. 62, No. 3, pp. 283-96. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB The principle of the radioallergosorbent test (RAST) has been used to measure IgG antibodies to timothy grass pollen allergens in sera from desensitized allergic subjects. 125I-labeled goat anti-human IgG was used as detector protein. Non-specific binding was eliminated by use of a non-porous nylon ball an antigen carrier and by use of a special buffer with high ionic strength and pH, containing 1% bovine gamma globulin and 5% normal rabbit serum as 'balance proteins'. At dilution 1:80 non-specific binding was only 0.28% and the binding ratio for a high-liter serum was about 10. By inhibition experiments the assay was demonstrated to be specific for IgG antibodies to timothy grass pollen. The results obtained with this assay correlated statistically significantly with those found th a double -antibody method (rs equal 0.68, n equal 20, t equal 3.93, P less than 0.001). Serum dilution curves were parallel, indicating that the assay is in allergen excess. The within-assay coefficient of variation ranged from 3.9 to 7.6%; the between-assay coefficient of variation from 8.4 to 19.5%. The assay is very simple to perform, requiring no centrifugation. The allergen -coated balls are stable for at least 3 months. The assay should be applicable to measurement of IgG antibodies and IgG subclass antibodies to any protein antigen of interest.

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L9         3031 ANTIGEN DELIVERY

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L10          89 L9 AND "E COLI"

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L11           5 L10 AND KILLED

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L12           3 DUP REMOVE L11 (2 DUPLICATES REMOVED)

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L12  ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
2003:530572  Document No.: PREV200300533511. Delivery of antigens to the
     cytosol of nonprofessional phagocytic cells using invasive Escherichia
     coli K-12 expressing listeriolysin O. Pratt, J. T. [Reprint Author];
     Higgins, D. E. [Reprint Author]. Harvard Medical School, Boston, MA, USA.
     Abstracts of the General Meeting of the American Society for Microbiology,
     (2003) Vol. 103, pp. E-109. http://www.asmusa.org/mtgsrc/generalmeeting.ht
     m. cd-rom.
     Meeting Info.: 103rd American Society for Microbiology General Meeting.
     Washington, DC, USA. May 18-22, 2003. American Society for Microbiology.
     ISSN: 1060-2011 (ISSN print). Language: English.
AB   Bacterial-based vectors can be used as vehicles for delivery of proteins
     to eukaryotic host cells.  The use of these vectors provides a distinct
     advantage because any protein that can be expressed by the bacteria can
     potentially be delivered without purification.  It has previously been
     shown that Escherichia coli expressing cytoplasmic recombinant
     listeriolysin O (LLO) can deliver antigenic protein to the cytosol of
     macrophages for processing and presentation through the MHC class I
     pathway.  LLO is a pore-forming cytolysin and an essential pathogenic
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determinant of Listeria monocytogenes. However, the E. coli/LLO delivery system has been limited to use in professional phagocytic cells (macrophages and dendritic cells). Therefore, we have modified the E. coli/LLO system to expand the delivery targets to nonprofessional phagocytic cells using an invasive strain of E. coli. We co-expressed LLO and invasin, an outer membrane protein from Yersinia pseudotuberculosis that mediates bacterial invasion through binding of host cell betal integrins, in an E. coli strain auxotrophic for peptidoglycan synthesis. Consequently, the E. coli induce phagocytosis through invasin-betal integrin interactions. Once inside the phagosome, bacteria undergo spontaneous lysis, releasing LLO and target proteins into the phagosome. Subsequent perforation of the phagosome by LLO allows the release of target proteins into the cytosol of host cells. Using T-cell activation assays, we have shown that both live and formalin-killed E. coli can efficiently deliver cytotoxic T-lymphocyte (CTL) antigens to the MHC class I presentation pathway of nonprofessional phagocytic cells. Furthermore, we have found that use of a peptidoglycan auxotroph is not required for efficient antigen delivery. In additional T-cell activation assays, E. coli without defects in peptidoglycan synthesis delivered antigen with approximately the same efficiency This system may facilitate the delivery of macromolecules to a wide variety of host cells and has the potential to be used as a delivery vector in a number of in vivo applications, including CTL stimulating vaccines and gene therapy.

L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
1999:243466 Document No. 131:43311 Delivery of protein to the cytosol of macrophages using Escherichia coli K-12. Higgins, Darren E.; Shastri, Nilabh; Portnoy, Daniel A. (Department of Molecular and Cell Biology, University of California, Berkeley, CA, 94720, USA). Molecular Microbiology, 31(6), 1631-1641 (English) 1999. CODEN: MOMIEE. ISSN: 0950-382X. Publisher: Blackwell Science Ltd..
AB Listeriolysin O (LLO) is an essential determinant of pathogenicity whose natural biol. role is to mediate lysis of Listeria monocytogenes containing phagosomes. In this study, we report that Escherichia coli expressing cytoplasmic recombinant LLO can efficiently deliver co-expressed proteins to the cytosol of macrophages. We propose a model in which subsequent or concomitant to phagocytosis the E. coli are killed and degraded within phagosomes causing the release of LLO and target proteins from the bacteria. LLO acts by forming large pores in the phagosomal membrane, thus releasing the target protein into the cytosol. Delivery was shown to be rapid, within minutes after phagocytosis. Using this method, a large enzymically active protein was delivered to the cytosol. Furthermore, we demonstrated that the E . coli/LLO system is very efficient for delivery of ovalbumin (OVA) to the major histocompatibility (MHC) class I pathway for antigen processing and presentation, greater than 4 logs compared with E . coli expressing OVA alone. Moreover, the time required for processing and presentation of an OVA-derived peptide was similar to that previously reported when purified OVA was introduced directly into the cytosol by other methods. Using this system, potentially large amts. of any protein that can be expressed in E. coli can be delivered to the cytosol without protein purification The potential use of this system for the delivery of antigenic protein in vivo and the delivery of DNA are discussed.

L12 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1
1998020885. PubMed ID: 9382741. Bacterial antigen delivery systems: phagocytic processing of bacterial antigens for

MHC-I and MHC-II presentation to T cells. Svensson M; Pfeifer J; Stockinger B; Wick M J. (Dept. of Cell and Molecular Biology, Lund University, Sweden.) Behring Institute Mitteilungen, (1997 Feb) No. 98, pp. 197-211. Ref: 49. Journal code: 0367532. ISSN: 0301-0457. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Using an in vitro model system we have studied parameters of both bacteria and antigen presenting cells that influence peptide presentation by murine major histocompatibility complex class II (MHC-II) and class I (MHC-I) molecules. To study MHC-II presentation, the HEL (52-61) epitope, which binds the murine MHC-II molecule I-Ak, was expressed as the cytoplasmic Crl-HEL fusion protein in S. typhimurium. When murine peritoneal macrophages mediated phagocytic processing of S. typhimurium expressing Crl-HEL, HEL (52-61) was processed and presented on I-Ak more efficiently from heat-killed S. typhimurium than from viable bacteria, and from a rough LPS strain compared to its isogenic smooth LPS counterpart, most likely due to enhanced phagocytosis of the rough LPS strain. Macrophages also processed phoP S. typhimurium strains with greater efficiency for peptide presentation by I-Ak than wild type bacteria while Salmonella constitutively expressing phoP were processed for peptide presentation by I-Ak less efficiently than wild type Salmonella. We have also shown that macrophage phagocytosis of E. coli or S. typhimurium results in presentation of bacterial antigens by MHC-I molecules. To investigate the role of post-Golgi MHC-I molecules in this presentation pathway, peritoneal macrophages from TAP1-/- mice, which are deficient in presenting endogenous antigens on MHC-I and lack significant surface MHC-I expression, were co-incubated with bacteria containing the 257-264 epitope from ovalbumin [OVA(257-264)], which binds the murine class I molecule Kb. Peritoneal macrophages from TAP1-/-/ mice could process bacteria expressing the OVA epitope for recognition by epitope-specific T hybridoma cells. This processing and presentation was reduced in efficiency between three to 100 fold compared to C57BL/6 macrophages, depending on the protein harbouring the OVA (257-264) epitope (Crl-OVA or native OVA). This suggests that the protein context of the OVA (257-264) epitope influences the extent of TAP-independent processing for MHC-I presentation. In addition, we show that murine bone marrow-derived dendritic cells can phagocytose and process viable gram negative bacteria for peptide presentation on MHC-I and MHC-II; inhibition studies showed that acidic compartments in dendritic cells are required for this presentation. These results suggest that dendritic cells may be potential antigen presenting cells used in eliciting specific immune responses against bacteria.

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L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2003:610197 Document No. 139:148468 Methods and composition for delivering nucleic acids and/or proteins to the respiratory system. Chen, Wei; Fu, Xiaoli; Nouraini, Sherry; Zhang, Zhiqing (Symbigene, Inc., USA). PCT Int. Appl. WO 2003063786 A2 20030807, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US2469 20030127. PRIORITY: US 2002-353885P

20020131; US 2002-353923P 20020131; US 2002-401465P 20020805; US 2002-280769 20021025.
AB Methods and compostions related to the fields of bacteriol., immunol. and gene therapy are provided. In general modified microflora for the delivery of vaccines, allergens and therapeutics to the mucosal surfaces of the respiratory tract are provided. In particular, the compns. and methods are directed at inducing an M-cell mediated immune response to pathogenic diseases. Specifically, methods of vaccine preparation, delivery and mucosal immunization using a Lactic Acid Bacteria (LAB), yeast and LAB that have been modified through fusion with E. coli to either present on its cell surface, or secrete, antigenic epitopes derived from pathogenic microorganisms and/or to secrete a therapeutic protein sequence are disclosed.

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L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2003:610197 Document No. 139:148468 Methods and composition for delivering nucleic acids and/or proteins to the respiratory system. Chen, Wei; Fu, Xiaoli; Nouraini, Sherry; Zhang, Zhiqing (Symbigene, Inc., USA). PCT Int. Appl. WO 2003063786 A2 20030807, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US2469 20030127. PRIORITY: US 2002-353885P 20020131; US 2002-353923P 20020131; US 2002-401465P 20020805; US 2002-280769 20021025.
AB Methods and compostions related to the fields of bacteriol., immunol. and gene therapy are provided. In general modified microflora for the delivery of vaccines, allergens and therapeutics to the mucosal surfaces of the respiratory tract are provided. In particular, the compns. and methods are directed at inducing an M-cell mediated immune response to pathogenic diseases. Specifically, methods of vaccine preparation, delivery and mucosal immunization using a Lactic Acid Bacteria (LAB), yeast and LAB that have been modified through fusion with E. coli to either present on its cell surface, or secrete, antigenic epitopes derived from pathogenic microorganisms and/or to secrete a therapeutic protein sequence are disclosed.

=> s l9 and modified allergen
L16 0 L9 AND MODIFIED ALLERGEN

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L17 60 ALLERGEN DELIVERY

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L19 1 L17 AND BACTERIA

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L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2001:676622 Document No. 135:225857 Microbial delivery system. Caplan, Michael (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2001066136 A2 20010913, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33121 20001206. PRIORITY: US 2000-PV195035 20000306.

AB The present invention provides methods and compns. for treating or preventing allergic responses, particularly anaphylactic allergic responses, in subjects who are allergic to allergens or susceptible to allergies. Methods of the present invention utilize administration of microorganisms to subjects, where the microorganisms produce allergens and protect the subjects from exposure to the allergens until phagocytosed by antigen-presenting cells. Particularly preferred microorganisms are gram-neg. bacteria, gram-pos. bacteria, and yeast. Particularly preferred allergens are proteins found in foods, venoms, drugs and latex that elicit allergic reactions and anaphylactic allergic reactions in individuals who are allergic to the proteins or are susceptible to allergies to the proteins. The proteins may also be modified to reduce the ability of the proteins to bind and crosslink IgE antibodies and thereby reduce the risk of eliciting anaphylaxis without affecting T-cell mediated Th1-type immunity.

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L20 155308 ALLERGEN

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L21 255 L20 AND REDUCED IGE BINDING

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L22 6 L21 AND BACTERIA

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PROCESSING COMPLETED FOR L22
L23 6 DUP REMOVE L22 (0 DUPLICATES REMOVED)

=> d l23 1-6 cbib abs

L23 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
2008:70107 Document No.: PREV200800062051. A hypoallergenic vaccine obtained by tail-to-head restructuring of timothy grass pollen profilin, Phl p 12, for the treatment of cross-sensitization to profilin. Westritschnig, Kerstin; Linhart, Birgit; Focke-Tejkl, Margarete; Pavkov, Tea; Keller, Walter; Ball, Tanja; Mari, Adriano; Hartl, Arnulf; Stoecklinger, Angelika; Scheiblhofer, Sandra; Thalhamer, Josef; Ferreira, Fatima; Vieths, Stefan; Vogel, Lothar; Boehm, Alexandra; Valent, Peter; Valenta, Rudolf [Reprint Author]. Med Univ Vienna, Vienna Gen Hosp, Ctr Physiol and Pathophysiol, Dept Pathol,Christian Doppler Lab Allergy Res, Wahringer Gurtel 18-20, A-1090 Vienna, Austria. Rudolf.valenta@meduniwien.ac.at. Journal of Immunology, (DEC 1 2007) Vol. 179, No. 11, pp. 7624-7634.

CODEN: JOIMA3. ISSN: 0022-1767. Language: English.

AB Profilins are highly cross-reactive allergens in pollens and plant food. In a paradigmatic approach, the cDNA coding for timothy grass pollen profilin, Phl p 12, was used as a template to develop a new strategy for engineering an allergy vaccine with low IgE reactivity. Non-IgE-reactive fragments of Phl p 12 were identified by synthetic peptide chemistry and restructured (rs) as a new molecule, Phl p 12-rs. It comprised the C terminus of Phl p 12 at its N terminus and the Phl p 12 N terminus at its C terminus. Phl p 12-rs was expressed in Escherichia coli and purified to homogeneity. Determination of secondary structure by circular dichroism indicated that the restructuring process had reduced the IgE-reactive alpha-helical contents of the protein but retained its beta-sheet conformation. Phl p 12-rs exhibited reduced IgE binding capacity and allergenic activity but preserved T cell reactivity in allergic patients. IgG Abs induced by immunization of mice and rabbits with Phl p 12-rs cross-reacted with pollen and food-derived profilins. Recombinant Phl p 12-rs, rPhl p 12-rs, induced less reaginic IgE to the wild-type allergen than rPhl p 12. However, the rPhl p 12-rs-induced IgGs inhibited allergic patients' IgE Ab binding to profilins to a similar degree as those induced by immunization with the wild type. Phl p 12-rs specific IgG inhibited profilin-induced basophil degranulation. In conclusion, a restructured recombinant vaccine was developed for the treatment of profilin-allergic patients. The strategy of tail-to-head reassembly of hypoallergenic allergen fragments within one molecule represents a generally applicable strategy for the generation of allergy vaccines.

L23 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

2007:243317 Document No.: PREV200700234468. Generation of a low Immunoglobulin E-binding mutant of the timothy grass pollen major allergen Phl p 5a. Wald, M. [Reprint Author]; Kahlert, H.; Weber, B.; Jankovic, M.; Keller, W.; Cromwell, O.; Nandy, A.; Fiebig, H.. Allergopharma J Ganzer KG, Res and Dev, Hermann Korner Str 52, D-21465 Reinbek, Germany. martin.wald@allergopharma.de. Clinical and Experimental Allergy, (MAR 2007) Vol. 37, No. 3, pp. 441-450. ISSN: 0954-7894. Language: English.

AB Immunotherapy of grass pollen allergy is currently based on the administration of pollen extracts containing natural allergens. Specifically designed recombinant allergens with reduced IgE reactivity could be used in safer and more efficacious future therapy concepts.This study aimed to generate hypoallergenic variants of the timothy grass major allergen Phl p 5a as candidates for allergen-specific immunotherapy.Three deletion mutants were produced in Escherichia coli and subsequently purified. The overall IgE-binding capacity of the mutants was compared with the recombinant wild-type allergen by membrane blot and IgE-inhibition assays. The capacity for effector cell activation was determined in basophil activation assays. T cell proliferation assays with allergen -specific T cell lines were performed to confirm the retention of T cell reactivity. Structural properties were characterized by circular dichroism analysis and homogeneity by native isoelectric focusing. The deletion sites were mapped on homology models comprising the N- and C-terminal halves of Phl p 5a, respectively.The double-deletion mutant rPhl p 5a Delta(94-113, 175-198) showed strongly diminished IgE binding in membrane blot and IgE-inhibition assays. Both deletions affect predominantly alpha-helical regions located in the N- and C-terminal halves of Phl p 5a, respectively. Whereas deletion of Delta 175-198 alone was sufficient to cause a large reduction of the IgE reactivity in a subgroup of allergic sera, only the combination of both deletions was highly effective for all the sera tested. rPhl p 5a Delta(94-113, 175-198) consistently showed at least an 11.5-fold reduced capacity to activate

basophils compared with the recombinant wild-type molecule, and the T cell proliferation assays demonstrated retention of T cell reactivity.The mutant rPh1 p 5a Delta(94-113, 175-198) fulfils the basic requirements for a hypoallergenic molecule suitable for a future immunotherapy of grass pollen allergy; it offers substantially reduced IgE binding and maintained T cell reactivity.

L23 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
2001:2594 Document No.: PREV200100002594. Effects of proline mutations in the major house dust mite allergen Der f 2 on IgE-binding and histamine-releasing activity. Takai, Toshiro [Reprint author]; Ichikawa, Saori; Hatanaka, Hideki; Inagaki, Fuyuhiko; Okumura, Yasushi. Bioscience Research and Development Laboratory, Asahi Breweries, Ltd, 1-21, Midori 1-chome, Moriya-machi, Kitasoma-gun, Ibaraki, 302-0106, Japan. toshiro.takai@asahibeer.co.jp. European Journal of Biochemistry, (November, 2000) Vol. 267, No. 22, pp. 6650-6656. print.
CODEN: EJBCAI. ISSN: 0014-2956. Language: English.
AB Der f 2 is the major group 2 allergen from house dust mite Dermatophagoides farinae and is composed of 129 amino-acid residues. Wild-type and six proline mutants of Der f 2 (P26A, P34A, P66A, P79A, P95A, and P99A) expressed in Escherichia coli were refolded and purified. Formations of intramolecular disulfide bonds in the purified proteins were confirmed correct. The apparent molecular masses analyzed by gel-filtration were 14-15 kDa. The IgE-binding capacity in the sera of seven mite-allergic patients, inhibitory activity for IgE-binding to immobilized wild-type Der f 2, and activity to stimulate peripheral blood basophils to release histamine in two volunteers were analyzed. P95A and P99A, which slightly differed from the wild-type Der f 2 in their CD spectrum, showed reduced IgE-binding, reduced inhibitory activity, and less histamine-releasing activity than the wild-type. P34A also showed reduced allergenicity. Considering that Pro95, Pro99 and Pro34 are closely located in loops at one end of the tertiary structure of Der f 2, we concluded that these loop regions included an IgE-binding site common to all tested patients. P66A showed reduced IgE-binding in two sera out of seven. P26A and P79A showed no reduced allergenicity. However, in immunoblot analysis after SDS/PAGE under reduced conditions, P79A showed no or markedly reduced IgE-binding while the other mutants showed IgE-binding corresponding to that in the assay using correctly refolded proteins. This suggests that Pro79 is involved in refolding of Der f 2. The findings in this study are important for the understanding of the antigenic structure of mite group 2 allergens and for manipulation of the allergens for specific immunotherapy.

L23 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine, University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2.
APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.
AB It has been determined that allergens, which are characterized by

both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compound that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut allergens to demonstrate alteration of IgE binding sites. The critical amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been determined Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most critical to IgE binding.

L23 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
1997:500865 Document No.: PREV199799800068. Molecular characterization, expression in Escherichia coli, and epitope analysis of a two EF-hand calcium-binding birch pollen allergen, Bet v 4. Twardosz, Anna; Hayek, Brigitte; Seiberler, Susanne; Vangelista, Luca; Elfman, Lena; Gronlund, Hans; Kraft, Dietrich; Valenta, Rudolf [Reprint author]. Inst. Gen. Exp. Pathol., AKH, Univ. Vienna, Vienna, Austria. Biochemical and Biophysical Research Communications, (1997) Vol. 239, No. 1, pp. 197-204. CODEN: BBRCA9. ISSN: 0006-291X. Language: English.
AB Birch pollen belongs to the most potent elicitors of Type I allergic reactions in early spring. Using serum IgE from a birch pollen allergic patient, two cDNA clones (clone 6 and clone 13) were isolated from a birch pollen expression cDNA library constructed in phage lambda-gt11. Clone 6 encoded a 9.3 kD two EF-hand calcium-binding protein, designated Bet v 4, with significant end to end sequence homology to EF-hand calcium-binding allergens from weed and grass pollen. Recombinant Bet v 4, expressed as beta-galactosidase fusion protein, reacted with serum IgE from approximately 20% of pollen allergic individuals. Depletion of allergen-bound calcium by EGTA treatment lead to a substantial reduction of IgE-binding to Bet v 4, indicating that protein-bound calcium is necessary for the maintenance of IgE-epitopes. The greatly reduced IgE-binding capacity of clone 13, a Bet v 4 fragment that lacked the 16 N-terminal amino acids, indicated that the N-terminus contributes significantly to the proteins IgE-binding capacity. By IgE-inhibition experiments it was demonstrated that recombinant Bet v 4 shared IgE-epitopes with natural Bet v 4 and a homologous timothy grass pollen allergen. Recombinant Bet v 4 may therefore be considered as a relevant crossreactive plant allergen, which may be used for diagnosis and treatment of patients suffering from multivalent plant allergies.

L23 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
1994:526700 Document No.: PREV199497539700. Complementary DNA cloning of the major allergen PhI p I from timothy grass (Phleum pratense); recombinant PhI p I inhibits IgE binding to group I allergens from eight different grass species. Laffer, Sylvia; Valenta, Rudolf; Vrtala, Susanne; Susani, Markus; Van Ree, Ronald; Kraft, Dietrich; Scheiner, Otto; Duchene, Michael [Reprint author]. Inst. General Experimental Pathology, AKH, Waehringergeutel 18-20, A-1090 Vienna, Austria. Journal of Allergy and Clinical Immunology, (1994) Vol. 94, No. 4, pp. 689-698.
CODEN: JACIBY. ISSN: 0091-6749. Language: English.
AB Background: Grass pollens, such as pollen from timothy grass (Phleum

pratense), represent a major cause of type I allergy. Objective: In this report we attempted to determine how cross-reactive allergenic components of grass pollens from different species can be represented by a minimum number of recombinant allergens. Methods: We isolated and sequenced a timothy grass pollen cDNA coding for the major allergen Phl p I. A recombinant Phl p I-beta-galactosidase fusion protein, which bound to IgE in 87% of patients with grass pollen allergy, was produced in Escherichia coli. Using recombinant Phl p V and Phl p I, we defined representative patients' sera that bound to group I but not to group V allergens, as well as sera with reactivity against group I and group V allergens. IgE immunoblot inhibition studies were done with nitrocellulose-blotted pollen extracts from eight grass species with different geographic distribution. Results: Preadsorption of patients' sera with recombinant nonfusion Phl p I strongly reduced IgE binding to group I allergens from the eight grasses. showing extensive cross-reactivity between species. Conclusion: A single recombinant group I allergen contains many of the IgE epitopes of group I isoallergens from a number of different grass species.

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=> s l21 and (E coli)
L24         10 L21 AND (E COLI)

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PROCESSING COMPLETED FOR L24
L25          3 DUP REMOVE L24 (7 DUPLICATES REMOVED)

=> d l26 1-3 cbib abs
L26 NOT FOUND
The L-number entered has not been defined in this session, or it
has been deleted.  To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

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L26          3 DUP REMOVE L25 (0 DUPLICATES REMOVED)

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L26  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
2007:1320549   Document No. 148:142264  A Hypoallergenic Vaccine Obtained by
     Tail-to-Head Restructuring of Timothy Grass Pollen Profilin, Phl p 12, for
     the Treatment of Cross-Sensitization to Profilin.  Westritschnig, Kerstin;
     Linhart, Birgit; Focke-Tejkl, Margarete; Pavkov, Tea; Keller, Walter;
     Ball, Tanja; Mari, Adriano; Hartl, Arnulf; Stoecklinger, Angelika;
     Scheiblhofer, Sandra; Thalhamer, Josef; Ferreira, Fatima; Vieths, Stefan;
     Vogel, Lothar; Boehm, Alexandra; Valent, Peter; Valenta, Rudolf (Christian
     Doppler Laboratory for Allergy Research, Division of Immunopathology,
     Department of Pathophysiology, Center for Physiology and Pathophysiology,
     Medical University of Vienna, Vienna, Austria).  Journal of Immunology,
     179(11), 7624-7634 (English) 2007.  CODEN: JOIMA3.  ISSN: 0022-1767.
     Publisher: American Association of Immunologists.
AB   Profilins are highly cross-reactive allergens in pollens and
     plant food.  In a paradigmatic approach, the cDNA coding for timothy grass
     pollen profilin, Phl p 12, was used as a template to develop a new
     strategy for engineering an allergy vaccine with low IgE reactivity.
     Non-IgE-reactive fragments of Phl p 12 were identified by synthetic
     peptide chemical and restructured (rs) as a new mol., Phl p 12-rs.  It
     comprised the C terminus of Phl p 12 at its N terminus and the Phl p 12 N
     terminus at its C terminus.  Phl p 12-rs was expressed in E.
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coli and purified to homogeneity. Determination of secondary structure by CD indicated that the restructuring process had reduced the IgE-reactive α-helical contents of the protein but retained its β-sheet conformation. Phl p 12-rs exhibited reduced IgE binding capacity and allergenic activity but preserved T cell reactivity in allergic patients. IgG Abs induced by immunization of mice and rabbits with Phl p 12-rs cross-reacted with pollen and food-derived profilins. Recombinant Phl p 12-rs, rPhl p 12-rs, induced less reaginic IgE to the wild-type allergen than rPhl p 12. However, the rPhl p 12-rs-induced IgGs inhibited allergic patients' IgE Ab binding to profilins to a similar degree as those induced by immunization with the wild type. Phl p 12-rs specific IgG inhibited profilin-induced basophil degranulation. Thus, a restructured recombinant vaccine was developed for the treatment of profilin-allergic patients. The strategy of tail-to-head reassembly of hypoallergenic allergen fragments within one mol. represents a generally applicable strategy for the generation of allergy vaccines.

L26 ANSWER 2 OF 3 MEDLINE on STN
94366422. PubMed ID: 7521933. Potential therapeutic recombinant proteins comprised of peptides containing recombined T cell epitopes. Rogers B L; Bond J F; Craig S J; Nault A K; Segal D B; Morgenstern J P; Chen M S; Bizinkauskas C B; Counsell C M; Lussier A M; +. (ImmuLogic Pharmaceutical Corporation, Waltham, MA 02154.) Molecular immunology, (1994 Sep) Vol. 31, No. 13, pp. 955-66. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The complete primary structure of Fel d I2 has been determined and shown to be comprised of two separate polypeptide chains (designated chain 1 and 2). Overlapping peptides covering the entire sequence of both chains of Fel d I have been used to map the major areas of human T cell reactivity. The present study describes three non-contiguous T cell reactive regions of < 30 aa in length that were assembled in all six possible configurations using PCR and recombinant DNA methods. These six recombinant proteins comprised of defined non-contiguous T cell epitope regions artificially combined into single polypeptide chains have been expressed in E. coli, highly purified, and examined for their ability to bind to human cat-allergic IgE and for human T cell reactivity. Several of these recombined T cell epitope-containing polypeptides exhibit markedly reduced IgE binding as compared to the native Fel d I. Importantly, the human T cell reactivity to individual T cell epitope-containing regions is maintained even though each was placed in an unnatural position as compared to the native molecule. In addition, T cell responses to potential junctional epitopes were not detected. It was also demonstrated in mice that s.c. injection of T cell epitope-containing polypeptides inhibits the T cell response to the individual peptides upon subsequent challenge in vitro. Thus, these recombined T cell epitope-containing polypeptides, which harbor multiple T cell reactive regions but have significantly reduced reactivity with allergic human IgE, constitute a novel potential approach for desensitization to important allergens.

L26 ANSWER 3 OF 3 MEDLINE on STN
93375976. PubMed ID: 8366858. Purification and immunochemical characterization of recombinant and native ragweed allergen Amb a II. Kuo M C; Zhu X J; Koury R; Griffith I J; Klapper D G; Bond J F; Rogers B L. (ImmuLogic Pharmaceutical Corporation, Waltham, MA.) Molecular immunology, (1993 Aug) Vol. 30, No. 12, pp. 1077-87. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The complete sequence of a cDNA encoding Amb a II and its relationship to

the Amb a I family of allergens has recently been described [Rogers et al. (1991) J. Immun. 147, 2547-2552; Griffith et al. (1991a), Int. Archs Allergy appl. Immun. 96, 296-304]. In this study, we present results generated with rabbit antipeptide antisera that recognize Amb a II or Amb a I, but not both. The specificity of two anti-Amb a II antipeptide sera, anti-RAE-50.K and anti-RAE-51.K, was verified on Western blots of recombinant Amb a II and Amb aI.1. These two sera, directed against separate regions of the Amb a II molecule, detected three individual 38-kDa Amb a II isoforms on 2D Western blots of aqueous ragweed pollen extract. These Amb a II isoforms have pI in the 5.5-5.85 range and can be easily distinguished from Amb a I isoforms with pI in the 4.5-5.2 range detected by an anti-Amb a I specific peptide antiserum. The Amb a II isoforms have also been individually purified from pollen, positively identified as Amb a II by amino acid sequencing, and visualized as separate bands on IEF gels. An analysis of Amb a II cDNA sequences generated by PCR led to the prediction of three Amb a II isoforms with pI of 5.74, 5.86 and 5.97 that are very similar to the pI deduced from 2D Western blot analysis. Recombinant Amb aI.1 and Amb a II have been expressed in E. coli, purified in their denatured form, and examined by ELISA for their capacity to bind pooled allergic human IgE. Purified native Amb a and Amb a II from pollen were shown to have very similar IgE-binding properties. In contrast, Amb a II had a markedly reduced IgE-binding capacity as compared to Amb a I.1. These data suggest that recombinant Amb a I.1 and Amb a II, isolated in a denatured form, differ significantly in their IgE-binding properties whereas the native molecules isolated from pollen do not.

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=> s "allergen delivery"
L27         60 "ALLERGEN DELIVERY"

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L28          2 L27 AND MUCOSAL

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PROCESSING COMPLETED FOR L28
L29           1 DUP REMOVE L28 (1 DUPLICATE REMOVED)

=> d l29 cbib abs

L29  ANSWER 1 OF 1     MEDLINE on STN                  DUPLICATE 1
2003483255.    PubMed ID: 14561171.   Respiratory tolerance in the protection
     against asthma. Macaubas Claudia; DeKruyff Rosemarie H; Umetsu Dale T.
     (Division of Immunology and Allergy, Department of Pediatrics, Stanford
     University, Stanford, CA 94305-5208, USA.. macaubas@stanford.edu) .
     Current drug targets. Inflammation and allergy, (2003 Jun) Vol. 2, No. 2,
     pp. 175-86.  Ref: 121. Journal code: 101160019. ISSN: 1568-010X. Pub.
     country: Netherlands. Language: English.
AB   Understanding the pathways involved in the induction and maintenance of
     respiratory tolerance to airborne allergens is important in designing new
     therapies for asthma and other allergic diseases that not only control
     disease symptoms, but also change or potentially cure the disease.
     Respiratory tolerance, and mucosal immunity are maintained by a
     complex system of defense mechanisms.  Most of the inhaled environmental
     load is eliminated by exclusion mechanisms, which include physical
     barriers, such as mucus, and cilia as well as a variety of mediators with
     anti-microbial and immunomodulatory properties.  Blanket immunosuppression
     is provided by alveolar macrophages, which inhibit antigen presentation
     and T cell responses, in addition to their role in pathogen elimination.
     Furthermore, there is antigen specific unresponsiveness or tolerance.
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This tolerance is mediated by lung dendritic cells producing IL-10, which induce the development of CD4+ T regulatory cells. The development of respiratory tolerance also depends on co-stimulation (CD86, and the ICOS-ICOSL pathway). Although exposure of the respiratory mucosa to some pathogenic agents (especially virus, and endotoxin) is associated with asthma exacerbations, microbial exposure may also promote mucosal tolerance and protection against the development of allergic diseases, but the mechanisms involved are not very well understood. Mucosal -based immunotherapy has been already used as an alternative form of allergen delivery in immunotherapy, the only available treatment that is able to reverse established allergic disease. Strategies to further improve mucosal immunotherapy include the use of modified allergen derived peptides, and adjuvants like CpG motifs.

=> s l27 and bacteria
L30 1 L27 AND BACTERIA

=> d l30 cbib abs

L30 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2001:676622 Document No. 135:225857 Microbial delivery system. Caplan, Michael (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2001066136 A2 20010913, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33121 20001206. PRIORITY: US 2000-PV195035 20000306.

AB The present invention provides methods and compns. for treating or preventing allergic responses, particularly anaphylactic allergic responses, in subjects who are allergic to allergens or susceptible to allergies. Methods of the present invention utilize administration of microorganisms to subjects, where the microorganisms produce allergens and protect the subjects from exposure to the allergens until phagocytosed by antigen-presenting cells. Particularly preferred microorganisms are gram-neg. bacteria, gram-pos. bacteria, and yeast. Particularly preferred allergens are proteins found in foods, venoms, drugs and latex that elicit allergic reactions and anaphylactic allergic reactions in individuals who are allergic to the proteins or are susceptible to allergies to the proteins. The proteins may also be modified to reduce the ability of the proteins to bind and crosslink IgE antibodies and thereby reduce the risk of eliciting anaphylaxis without affecting T-cell mediated Th1-type immunity.

=> s l27 and E coli
L31 0 L27 AND E COLI

=> s l27 and heat killed
L32 0 L27 AND HEAT KILLED

=> s (caplan m?/au)
L33 1507 (CAPLAN M?/AU)

=> s l33 and microbial delivery
L34 1 L33 AND MICROBIAL DELIVERY

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=> d l34 cbib abs

L34  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2001:676622   Document No. 135:225857  Microbial delivery
     system.  Caplan, Michael (Panacea Pharmaceuticals, LLC, USA).
     PCT Int. Appl. WO 2001066136 A2 20010913, 57 pp.  DESIGNATED STATES: W:
     AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU,
     CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
     IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
     MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
     TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
     TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA,
     GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
     (English).  CODEN: PIXXD2.  APPLICATION: WO 2000-US33121 20001206.
     PRIORITY: US 2000-PV195035 20000306.
AB   The present invention provides methods and compns. for treating or
     preventing allergic responses, particularly anaphylactic allergic
     responses, in subjects who are allergic to allergens or susceptible to
     allergies.  Methods of the present invention utilize administration of
     microorganisms to subjects, where the microorganisms produce allergens and
     protect the subjects from exposure to the allergens until phagocytosed by
     antigen-presenting cells.  Particularly preferred microorganisms are
     gram-neg. bacteria, gram-pos. bacteria, and yeast.  Particularly preferred
     allergens are proteins found in foods, venoms, drugs and latex that elicit
     allergic reactions and anaphylactic allergic reactions in individuals who
     are allergic to the proteins or are susceptible to allergies to the
     proteins.  The proteins may also be modified to reduce the ability of the
     proteins to bind and crosslink IgE antibodies and thereby reduce the risk
     of eliciting anaphylaxis without affecting T-cell mediated Th1-type
     immunity.


=> s l33 and E coli
L35         10 L33 AND E COLI

=> s l35 and modified
L36          0 L35 AND MODIFIED

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PROCESSING COMPLETED FOR L35
L37          3 DUP REMOVE L35 (7 DUPLICATES REMOVED)

=> d l37 1-3 cbib abs

L37  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:259357   Document No. 142:334946  Recombinant allergens with mutated IgE
     epitopes for treating anaphylaxis induced by food, venom, drug and latex
     allergens.  Caplan, Michael J.; Bottomly, Kim H.; Sosin, Howard
     B.; Burks, A. Wesley; Sampson, Hugh A. (USA).  U.S. Pat. Appl. Publ. US
     20050063994 A1 20050324, 117 pp., Cont.-in-part of U.S. Ser. No. 100,303.
     (English).  CODEN: USXXCO.  APPLICATION: US 2004-899551 20040726.
     PRIORITY: US 2000-195035P 20000406; US 2000-731375 20001206; US
     2002-100303 20020318.
AB   The present invention provides methods and compns. for treating or
     preventing allergic reactions, particularly anaphylactic reactions.
     Methods of the present invention involve administering microorganisms to
     allergic subjects, where the microorganisms contain a recombinant version
     of the protein allergen.  The recombinant version can be wild-type or may
     include mutations within IgE epitopes of the protein allergen.  Preferably
     the compns. are administered rectally.  Particularly preferred
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microorganisms are bacteria such as E. coli . Any allergen may be used in the inventive methods. Particularly preferred allergens are anaphylactic allergens including protein allergens found in foods, venoms, drugs and latex. The inventive compns. and methods are demonstrated in the treatment of peanut-induced anaphylaxis.

L37 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1
1999394992. PubMed ID: 10464133. Bifidobacterial supplementation reduces the incidence of necrotizing enterocolitis in a neonatal rat model. Caplan M S; Miller-Catchpole R; Kaup S; Russell T; Lickerman M; Amer M; Xiao Y; Thomson R Jr. (Department of Pediatrics, Northwestern University Medical School, Evanston Hospital, Evanston, Illinois, USA.) Gastroenterology, (1999 Sep) Vol. 117, No. 3, pp. 577-83. Journal code: 0374630. ISSN: 0016-5085. Pub. country: United States. Language: English.
AB BACKGROUND & AIMS: Neonatal necrotizing enterocolitis (NEC) is a devastating gastrointestinal disease of premature infants partly caused by intestinal bacterial proliferation. Because bifidobacteria are thought to reduce the risk for intestinal disturbances associated with pathogenic bacterial colonization, we hypothesized that exogenous bifidobacterial supplementation to newborn rats would result in intestinal colonization and a reduction in the incidence of neonatal NEC. METHODS: Newborn rat pups were given Bifidobacterium infantis (10(9) organisms per animal daily), Escherichia coli, or saline control and exposed to the NEC protocol consisting of formula feeding (Esbilac; 200 cal. kg(-1). day(-1)) and asphyxia (100% N(2) for 50 seconds followed by cold exposure for 10 minutes). Outcome measures included stool and intestinal microbiological evaluation, gross and histological evidence of NEC, plasma endotoxin concentration, intestinal phospholipase A(2) expression, and estimation of intestinal mucosal permeability. RESULTS: Bifidobacterial supplementation resulted in intestinal colonization by 24 hours and appearance in stool samples by 48 hours. Bifidobacteria-supplemented animals had a significant reduction in the incidence of NEC compared with controls and E. coli-treated animals (NEC, 7/24 B. infantis vs. 19/27 control vs. 16/23 E. coli; P < 0.01). Plasma endotoxin and intestinal phospholipase A(2) expression were lower in bifidobacteria-treated pups than in controls, supporting the role of bacterial translocation and activation of the inflammatory cascade in the pathophysiology of NEC. CONCLUSIONS: Intestinal bifidobacterial colonization reduces the risk of NEC in newborn rats.

L37 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
95073279. PubMed ID: 7982271. Altered mitochondrial redox responses in gram negative septic shock in primates. Simonson S G; Welty-Wolf K; Huang Y T; Griebel J A; Caplan M S; Fracica P J; Piantadosi C A. (Department of Medicine, Duke University Medical Center, Durham, NC 27710.) Circulatory shock, (1994 May) Vol. 43, No. 1, pp. 34-43. Journal code: 0414112. ISSN: 0092-6213. Pub. country: United States. Language: English.
AB Gram negative sepsis causes changes in oxygen supply-demand relationships. We have used a primate model of hyperdynamic gram negative sepsis produced by intravenous infusion of Escherichia coli (E. coli) to evaluate sepsis-induced alterations in mitochondrial oxidation-reduction (redox) state in muscle in vivo. The redox state of cytochrome a,a3, the terminal member of the intramitochondrial respiratory chain, was assessed in the intact forearm by near-infrared (NIR) spectroscopy. The muscle NIR data were compared to routine measures of oxygen delivery (DO2) and oxygen consumption (VO2). After E. coli infusion and fluid resuscitation, DO2 and VO2 showed minimal changes through 24 hr of sepsis. In contrast, changes in cytochrome a,a3 redox state evaluated by NIR occurred within a few hours and were progressive. Mitochondrial functional responses were correlated with structural changes observed on serial muscle biopsies. Gross

morphological changes in muscle mitochondria were present in some animals as early as 12 hr, and, in most animals, by 24 hr. The morphologic changes were consistent with decreases in oxidative capacity as suggested by NIR spectroscopy. The NIR data also suggest that two mechanisms are operating to explain abnormalities in oxygen metabolism and mitochondrial function in lethal sepsis. These mechanisms include an early defect in oxygen provision to mitochondria that is followed by a progressive loss in functional cytochrome a,a3 in the muscle.

=> s l33 and allergen
L38 14 L33 AND ALLERGEN

=> dup remove l38
PROCESSING COMPLETED FOR L38
L39 14 DUP REMOVE L38 (0 DUPLICATES REMOVED)

=> d l39 1-14 cbib abs

L39 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2005:259357 Document No. 142:334946 Recombinant allergens with mutated IgE epitopes for treating anaphylaxis induced by food, venom, drug and latex allergens. Caplan, Michael J.; Bottomly, Kim H.; Sosin, Howard B.; Burks, A. Wesley; Sampson, Hugh A. (USA). U.S. Pat. Appl. Publ. US 20050063994 A1 20050324, 117 pp., Cont.-in-part of U.S. Ser. No. 100,303. (English). CODEN: USXXCO. APPLICATION: US 2004-899551 20040726. PRIORITY: US 2000-195035P 20000406; US 2000-731375 20001206; US 2002-100303 20020318.
AB The present invention provides methods and compns. for treating or preventing allergic reactions, particularly anaphylactic reactions. Methods of the present invention involve administering microorganisms to allergic subjects, where the microorganisms contain a recombinant version of the protein allergen. The recombinant version can be wild-type or may include mutations within IgE epitopes of the protein allergen. Preferably the compns. are administered rectally. Particularly preferred microorganisms are bacteria such as E. coli . Any allergen may be used in the inventive methods. Particularly preferred allergens are anaphylactic allergens including protein allergens found in foods, venoms, drugs and latex. The inventive compns. and methods are demonstrated in the treatment of peanut-induced anaphylaxis.

L39 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2003:855391 Document No. 139:363577 Modified anaphylactic food allergens with reduced IgE-binding ability for decreasing clinical reaction to allergy. Caplan, Michael J.; Sosin, Howard B.; Sampson, Hugh; Bannon, Gary A.; Burks, A. Wesley; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Soheila J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (USA). U.S. Pat. Appl. Publ. US 20030202980 A1 20031030, 194 pp., Cont.-in-part of U.S. Ser. No. 494,096. (English). CODEN: USXXCO. APPLICATION: US 2002-100303 20020318. PRIORITY: US 1995-9455P 19951229; US 1996-717933 19960923; US 1998-73283P 19980131; US 1998-74633P 19980213; US 1998-74624P 19980213; US 1998-74590P 19980213; US 1998-106872 19980629; US 1998-141220 19980827; US 1998-191593 19981113; US 1999-241101 19990129; US 1999-240557 19990129; US 1999-248674 19990211; US 1999-248673 19990211; US 1999-122560P 19990302; US 1999-122565P 19990302; US 1999-122566P 19990302; US 1999-122450P 19990302; US 1999-122452P 19990302; US 1999-267719 19990311; US 2000-494096 20000128.
AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to

be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a modified allergen with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, modified allergens are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The immunotherapeutics can be prepared in transgenic plants or animals; and administered in injection, aerosol, sublingual or topical form. The immunotherapeutics can also be encoded in gene for gene therapy and delivered by injecting into muscle or skin to induce tolerance. The Examples provided herein use peanut allergens to illustrate applications of the invention.

L39 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

2003:906632 Correction of: 2002:736063 Document No. 139:349665 Correction of: 137:277814 Modified anaphylactic food allergens with reduced IgE-binding ability for decreasing clinical reaction to allergy. Caplan, Michael; Sosin, Howard; Sampson, Hugh; Bannon, Gary A.; Burks, Wesley A.; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Sohelia J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (Panacea Pharmaceuticals, USA; et al.). PCT Int. Appl. WO 2002074250 A2 20020926, 299 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9108 20020318. PRIORITY: US 2001-276822P 20010316.

AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a modified allergen with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, modified allergens are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The

Examples provided herein use peanut allergens to illustrate applications of the invention.

L39 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2002:123512 Document No. 136:182453 IgE-blocking agents for passive desensitization. Caplan, Michael J. (USA). U.S. Pat. Appl. Publ. US 20020018778 A1 20020214, 22 pp., Cont.-in-part of U.S. Ser. No. 455,294. (English). CODEN: USXXCO. APPLICATION: US 2000-731221 20001206. PRIORITY: US 1999-455294 19991206; US 2000-213765P 20000623; US 2000-235797P 20000927.

AB IgE-blocking agents and methods of their use have been developed for desensitizing an individual to an antigen. These IgE-blocking agents work by blocking the antigen-binding site of the IgE mols. and thereby preventing the antigen from binding. These agents typically have up to one IgE binding site present per mol. so as prevent any crosslinking of IgE which could lead to an allergic reaction. The IgE-blocking agents include allergen epitope, antibody, or Ig. fragment. Methods of using these novel IgE blocking agents include administering the agents to alleviate or prevent allergic reactions as well as administering the agents to decrease the risk of allergic reactions during immunotherapy or "rush" immunotherapy. The IgE-blocking agents may be combined with immune adjuvant or cytokine for treatment. Compns. and kits comprising these IgE binding agents are also provided.

L39 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
2001:559717 Document No.: PREV200100559717. Methods to block IGE binding to cell surface receptors of mast cells. Caplan, Michael [Inventor]; Sosin, Howard [Inventor, Reprint author]. Fairfield, CT, USA. ASSIGNEE: Panacea Pharmaceuticals, LLC. Patent Info.: US 6299875 20011009. Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 9, 2001) Vol. 1251, No. 2. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB Compositions are administered to block IgE binding to receptors and ultimately displace native IgE from mast cells and related cell types, to prevent the activation of these cells during an allergic response. The compositions consist of a pharmaceutically acceptable carrier for systemic or local administration and an amount of compound binding specifically to the FcepsilonRI IgE binding sites, and more preferably, FcepsilonRI and FcepsilonRII IgE binding sites, to prevent activation and degranulation of mast cells in response to exposure to allergens. The compounds can consist of IgE molecules and fragments and modifications thereof, such as IgE fragments, humanized or single chain IgE antibodies or fragments thereof, IgE with a modified Fab, non-crosslinkable IgE, or peptidomimetics which bind to the same site on the receptor as the IgE, jointly referred to herein as "IgE fragments" unless otherwise stated.

L39 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2001:676622 Document No. 135:225857 Microbial delivery system. Caplan, Michael (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2001066136 A2 20010913, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33121 20001206. PRIORITY: US 2000-PV195035 20000306.

AB The present invention provides methods and compns. for treating or preventing allergic responses, particularly anaphylactic allergic

responses, in subjects who are allergic to allergens or susceptible to allergies. Methods of the present invention utilize administration of microorganisms to subjects, where the microorganisms produce allergens and protect the subjects from exposure to the allergens until phagocytosed by antigen-presenting cells. Particularly preferred microorganisms are gram-neg. bacteria, gram-pos. bacteria, and yeast. Particularly preferred allergens are proteins found in foods, venoms, drugs and latex that elicit allergic reactions and anaphylactic allergic reactions in individuals who are allergic to the proteins or are susceptible to allergies to the proteins. The proteins may also be modified to reduce the ability of the proteins to bind and crosslink IgE antibodies and thereby reduce the risk of eliciting anaphylaxis without affecting T-cell mediated Th1-type immunity.

L39 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

2001:416973 Document No. 135:45198 Prevention of an anaphylactic response to food allergens. Bannon, Gary A.; Burks, Wesley A.; Caplan, Michael J.; Sampson, Hugh; Sosin, Howard (Panacea Pharmaceuticals, LLC, USA; University of Arkansas; Mount Sinai School of Medicine, University of New York). PCT Int. Appl. WO 2001040264 A2 20010607, 100 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33124 20001206. PRIORITY: US 1999-455294 19991206; US 2000-PV213765 20000623; US 2000-PV235797 20000927.

AB The authors disclose methods for reducing allergic responses in individuals sensitive to one or more food antigens. In general, desensitization is achieved by administration of fragments of antigens characterized by a reduced ability to bind to their cognate IgE. In one example, mice were sensitized to peanut allergens by intragastric feeding. Administration of peptide fragments of Ara h 2, or an allergen mutein with altered IgE binding sites, abrogated an increase in IgE levels and anaphylactic sequelae.

L39 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

2001:416792 Document No. 135:10056 Controlled delivery of antigens. Caplan, Michael; Burks, Wesley A., Jr.; Bannon, Gary A. (The Board of Trustees of the University of Arkansas, USA; Panacea Pharmaceuticals, LLC). PCT Int. Appl. WO 2001039800 A2 20010607, 34 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US42607 20001206. PRIORITY: US 1999-PV169330 19991206.

AB Formulations and methods are developed for delivering antigens to individuals in a manner that substantially reduces contact between the antigen and IgE receptors displayed on the surfaces of cells involved in mediating allergic responses, which target delivery of antigen to dendritic, phagocytic and antigen presenting cells (APCs), and which have improved pharmacokinetics. By reducing direct and indirect association of antigens with antigen-specific IgE antibodies, the risk of an allergic reaction, possibly anaphylactic shock, is reduced or eliminated.

Particularly preferred antigens are those that may elicit anaphylaxis in individuals, including food antigens, insect venom and rubber-related antigens. In the preferred embodiments, the compns. include one or more antigens in a delivery material such as a polymer, in the form of particles or a gel, or lipid vesicles or liposomes, any of which can be stabilized or targeted to enhance delivery. Preferably, the antigen is surrounded by the encapsulation material. Alternatively or addnl., the antigen is displayed on the surface of the encapsulation material. One result of encapsulating antigen is the reduction in association with antigen-specific IgE antibodies. In some embodiments, antigens are stabilized or protected from degradation until the antigen can be recognized and endocytized by APCs which are involved in eliciting cellular and humoral immune responses. In a preferred embodiment, the formulation is designed to deliver antigens to individuals in a manner designed to promote a Th1-type mediated immune response and/or in a manner designed to suppress a Th2 response. In still another embodiment, the formulation effects preferential release of the antigen within APCs. For example, various synthetic, biodegradable polymeric microsphere formulations were prepared containing peanut allergen. Microspheres based on poly(lactide-co-glycolide) (75:25) containing an acid end group (0.1% loaded with allergen) had the lowest amount (<20 ng) of peanut protein detected on the outside of the microsphere and the best range of peanut protein allergens contained within the microspheres (having mol. wts. ranging from 15 kDa to 70 kDa).

L39 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2001:416791 Document No. 135:32734 Passive desensitization. Caplan, Michael (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2001039799 A2 20010607, 76 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33125 20001206. PRIORITY: US 1999-455294 19991206; US 2000-PV213765 20000623; US 2000-PV235797 20000927.
AB IgE-blocking agents and methods of their use have been developed for desensitizing an individual to an antigen. These IgE-blocking agents work by blocking the antigen-binding site of the IgE mols. and thereby preventing the antigen from binding. These agents typically have up to one IgE binding site present per mol. so as to prevent any crosslinking of IgE which could lead to an allergic reaction. Methods of using these novel IgE blocking agents include administering the agents to alleviate or prevent allergic reactions as well as administering the agents to decrease the risk of allergic reactions during immunotherapy or "rush" immunotherapy. Compns. and kits comprising these IgE binding agents are also provided.

L39 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2000:741936 Document No. 133:308997 Methods for skewing the balance between Th1 and Th2 immune responses. Bottomly, H. Kim; Caplan, Michael J.; Sosin, Howard B. (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2000061157 A1 20001019, 76 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,

PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US9270 20000407. PRIORITY: US 1999-290029 19990409.

AB The present invention provides compns. and methods for regulating immune system reactions by biasing T cell responses away from Th1 or Th2 responses in a pre-determined manner. Control is effected at the stage of antigen/APC encounter and/or at the stage of APC/T cell encounter. In preferred embodiments, a Th1 or Th2 response is inhibited through induction of the alternative response. The inventive methods and reagents are particularly useful for the management of autoimmune disorders, allergy, and asthma.

L39 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

2000:666624 Document No. 133:251267 Immunostimulatory nucleic acids and antigens. Sosin, Howard B.; Caplan, Michael J. (Panacea Pharmaceuticals, Llc, USA). PCT Int. Appl. WO 2000054803 A2 20000921, 103 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US7213 20000316. PRIORITY: US 1999-PV124595 19990316; US 1999-PV125071 19990317.

AB The present invention provides methods and compns. for modulating an individual's immune response to antigens. It is an aspect of the present invention that allergic responses to antigens, which in some cases lead to asthma and even anaphylaxis, can be treated or prevented by administering compns. having immunostimulatory oligonucleotides having unmethylated CpG sequences. It is another aspect of the present invention that allergies to antigens, especially one that result in asthma and anaphylaxis, can be treated or prevented by administering compns. containing immunostimulatory oligonucleotides having unmethylated CpG dinucleotide sequences and further comprising antigen(s), fragments of the antigen, mixts. of fragments of the antigen, antigens modified to reduce Th2-type immune responses, and fragments of the antigen modified to reduce Th2-type immune responses. Cellular systems for studying immunostimulation by CpG containing nucleic acids include in vivo, in vitro or ex vivo systems.

L39 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN

2000:573822 Document No. 133:163051 Method for altering immune responses to polypeptides. Caplan, Michael (Panacea Pharmaceuticals, Llc, USA). PCT Int. Appl. WO 2000047610 A2 20000817, 49 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US3448 20000210. PRIORITY: US 1999-247406 19990210.

AB The author discloses methodol. for altering undesirable immune responses to polypeptides by their recombinant engineering. Such polypeptides are safer and can be more efficacious when introduced into a human, other mammal, or other animal. The disclosed method involves providing a collection of mutant polypeptides where the amino acid sequence of each mutant polypeptide differs in at least one position from a polypeptide of interest. Mutant polypeptides that exhibit less of the immune response than the polypeptide of interest, but still retain desired characteristic(s) are then identified. The collection of mutant polypeptides is provided by mutagenizing nucleic acid encoding a

polypeptide and expressing the mutagenized nucleic acid.

L39 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
2000:420987 Document No. 133:57594 Decreasing allergic reactions by inhibition of IgE binding. Caplan, Michael; Sosin, Howard (USA). PCT Int. Appl. WO 2000035484 A2 20000622, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US30238 19991217. PRIORITY: US 1998-216117 19981218.
AB The authors disclose methodol. for preventing allergic response by the inhibition of IgE binding to its epitopes on cognate allergens. Mols. which bind to these epitopes can be identified and synthesized and then formulated to coat or blend with the allergenic components to prevent IgE binding. In one example, the inhibitory mols. are IgE fragments selected using phage display technol. In a second example, the masking reagents are CDR-derived peptides or peptidomimetics which bind to the relevant epitopes on the allergens.

L39 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
1999:783962 Document No. 132:22180 Compounds binding specifically to FcεRI IgE binding sites for pan-specific anti-allergy therapy. Caplan, Michael; Sosin, Howard (USA). PCT Int. Appl. WO 9962550 A1 19991209, 28 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US12526 19990604. PRIORITY: US 1998-90375 19980604.
AB Compns. are administered to block IgE binding to receptors and ultimately displace native IgE from mast cells and related cell types, to prevent the activation of these cells during an allergic response. The compns. consist of a pharmaceutically acceptable carrier for systemic or local administration and an amount of compound binding specifically to the FcεRI IgE binding sites, and more preferably, FcεRI and FcεRII IgE binding sites, to prevent activation and degranulation of mast cells in response to exposure to allergens. The compds. can consist of IgE mols. and fragments and modifications thereof, such as IgE fragments, humanized or single chain IgE antibodies or fragments thereof, IgE with a modified Fab, non-cross-linkable IgE, or peptidomimetics which bind to the same site on the receptor as the IgE, jointly referred to herein as "IgE fragments" unless otherwise stated.